REMARKS/ARGUMENTS

This paper is filed in response to the Office Action of December 13, 2004. In the Office Action, the Examiner partially withdrew the Restriction Requirement originally received in the case, allowing claim 26 to be examined with the elected claims. Thus, claims 1-21, 26, and 31-37 were examined on the merits. Claims 8-15 and 33-37 were objected to as being substantial duplicates of claims 1-7 and 33-37. Claim 13 was objected to as being a substantial duplicate of claim 12. Claims 1-21, 26, and 31-37 were rejected under 35 U.S.C. §112, second paragraph as being indefinite. Claims 1-5, 8-13, 21, and 31 were rejected under 35 U.S.C. §102(b) as being anticipated by *Topographical control of cell behaviour: II. multiple grooved substrata,* (hereinafter "Clark"). Clark, *et al., Development,* 108, 635-64 (1990). Claims 1-19, 21, 26, and 31-37 were also rejected under 35 U.S.C. §103(a) as being unpatentable over U.S. Patent No.: 5,858,721 to Naughton, *et al.,* (hereinafter "Naughton") in view of Clark and U.S. Patent Nos: 6,419,491 and 4,832,759, to Ricci *et al.,* and Curtis *et al.,* respectively (hereinafter "Ricci" and "Curtis"). Claim 21 was rejected under 35 U.S.C. §103(a) in view of Naughton, Clark, Ricci, Curtis, and U.S. Patent No.: 4,940,853 to Vandenburgh (hereinafter "Vandenburgh").

By this paper, claims 1, 5, 8, 10, 16, 17, 19-21, 31, 32, 36, and 37 have been amended. Claims 4 and 11 were cancelled. Claims 22-25 and 27-30 are withdrawn. Claims 38 and 39 have been presented to assure appropriate coverage of the present invention by the claims. These claims are supported by various portions of the specification including, for example, Example 6, page 52, and Figures 2, and 10-12. Thus, claims 1-21, 26, and 31-37 are presented for the reconsideration of the Examiner in light of the above amendments with the following arguments.

Claim Objections

The Examiner entered several rejections to the claims as amended in the response to the restriction requirement. The first objection is to claims 8-15 and 33-37 being "substantial duplicate[s]" of claims 1-7 and 33-37. Office Action, p. 3. By this paper, claims 1 and 8 have been amended, and now differ in scope. Difference in scope is sufficient to meet the requirements of 37 C.F.R. §1.75. *See, e.g.,* MPEP 706.03(k).

The next objection is to claims 12 and 13 as being substantial duplicates. Applicants note that as originally submitted, claim 12 recites a device including a bioartificial composite having "an over all planar shape," while claim 13 recites a device with a bioartificial composite having "an over all **non**-planar shape." *(Emphasis added.)* The planar/non-planar terms originally submitted give claims and 13 differing scopes, and as a result, that this objection is not supported by MPEP 706.03(k). Applicants respectfully request withdrawal of this objection.

Claim Rejections – 35 U.S.C. §112

The Examiner rejected claims 1-21, 26, and 31-37 under 35 U.S.C. §112, second paragraph as being indefinite for "failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention." Office Action, p. 4. The MPEP explains that:

> Definiteness of claim language must be analyzed, not in a vacuum, but in light of:
> (A) The content of the particular application disclosure;
> (B) The teachings of the prior art; and
> (C) The claim interpretation that would be given by one possessing the ordinary level of skill in the pertinent art at the time the invention was made.

MPEP §2173.02. Applicants believe that in light of the disclosure provided in the instant specification and the level of understanding of one of ordinary skill in the art, these rejections are improper, and should be withdrawn.

The Examiner rejected claim 1, asserting that the term "cytoskeletal elements aligned uniformly" was "uncertain as to meaning and scope." *Id.* By this paper, claim 1 has been amended to clarify the alignment of the cytoskeletal elements of the cells propagated on the devices of the present invention. Further, pages 23, and 35-36, among others, discuss the "scope" of this orientation, and the cellular components considered to make up the cytoskeleton which are aligned in the devices of the present invention. Applicants respectfully request the withdrawal of this rejection.

The Examiner rejected claim 1, asserting that the term "layer oriented in the direction of said first layer" is "uncertain as to meaning and scope." Office Action, p. 4. Applicants believe that the amendment of claim 1 presented above to clarify the orientation of the first layer of cells overcomes this rejection.

Claim 1 was further rejected by the Examiner as being "unclear as to the difference in the first and second layers since how the second layer is produced has not been specified." Office Action, p. 4. Applicants question the need for including potential methods for producing this second layer of cells in the claims. The specification notes that the second layer may be produced by growth of second and potentially subsequent layers of tissue onto a device implanted into an organism with a first layer of cells already present, as well as the *ex vivo* deposition and development of a second layer of cells. *See, e.g.,* Specification, p. 16, lines 25-31. In order to advance the prosecution of the case, claim 1 has been amended to recite that the second layer of cells is "later-deposited" onto the first layer. Applicants request withdrawal of this rejection.

The Examiner next rejected claim 2 and others using the "root mean squared" term as a measure of surface roughness. In the field of surface texture, the term root mean square is commonly used in the art to describe average surface roughness. *See, e.g.,* Fundamentals of Modern Manufacturing, Materials, Processes and Systems, Groover, (1999), pp. 90-92 provided herewith as Exhibit A. Applicants thus respectfully request that this rejection be withdrawn.

The rejection of claim 3 and others discussing the measure of surface curvature requests further information as to how this would be recognized or measured. This measure of surface curvature refers to the minimal trough size that must be expressed on the substrate surface according to the present invention.

Claims 16 and 17 have been amended to address the Examiner's rejection relating to the substrate referred to in claims 16-18. Applicants believe that these amendments specifically reference the substrate listed in claim 8, and thus overcome the rejection.

Claims 19 and 20 have been amended remove the language cited by the Examiner in light of the amendments previously made to claim 8, and also to address the antecedent basis issues raised by the Examiner relating to the cell layers stated in the claims. These claims have further been amended to remove the "morphological rearrangement" language cited by the Examiner.

The Examiner next rejected claims 5, 12, and 13 as containing language that is "uncertain as to meaning and scope." Applicants have modified this language to address the Examiner's concerns, stating that the substrates are "substantially" planar or non-planar. Examples of

suitable substrates for each category are provided in the specification of the present invention, including at page 11, lines 4-11 and 20-25, and demonstrated in the examples, including Example I. Applicants request withdrawal of this rejection.

With regard to the rejection of claim 20 relating to the term "force" used in the claim, Applicants refer the Examiner to the Specification, including page 12, lines 9-21, where the use of stretching forces, and fluid pressures on the substrate or surface are noted to promote cell orientation and alignment. Applicants request withdrawal of this rejection.

Claim 21 has been amended to denote that it is a claim drawn to the preparation of the substrate of the device presented in claims 1 or 8.

Claims 4 and 11 have been deleted in response to the Examiner's rejection.

Claim 31 has been amended to explain the origin of cells included in the cellular preparation referred to.

Claim 32 has been amended to overcome the antecedent basis issues raised by the Examiner.

Claim 36 has been amended to provide the full spelling of "central nervous system" or "CNS."

Claim 37 has been amended as suggested by the Examiner to properly set forth a Markush group.

In light of the above amendments, cancellations, and arguments, the Applicants believe that the rejections made under 35 U.S.C. §112 have been overcome and respectfully request their withdrawal.

Claim Rejections – 35 U.S.C. §102

Claims 1-5, 8-13, 21, and 31 were rejected by the Examiner under 35 U.S.C. §102(b) as being anticipated by Clark. For a reference to anticipate a claim under 35 U.S.C. §102(b), "each and every element as set forth in the claim [must be] found, either expressly or inherently described, in a single prior art reference." *Verdegaal Bros. v. Union Oil Co. of California,* 814 F.2d 628, 631 (Fed. Cir. 1987), *cited in* MPEP §2131. The MPEP further clarifies that "[t]he identical invention must be shown in as complete detail as is contained in the claim." MPEP

§2131, *quoting Richardson v. Suzuki Motor Co.*, 868 F.2d 1226, 1236, 9 USPQ2d 1913, 1920 (Fed. Cir. 1989). Claims 1 and 8 have been amended above to note that surface topography provided on some of the claimed devices has "non-uniform grooves substantially aligned with the axis of the substrate." Claims 1 and 8, *supra*. Applicants submit that such surface topographies are not provided by the references given by the Examiner, and thus, that the claims as amended herein are not anticipated. Applicants thus request that this rejection be withdrawn.

Clark teaches the provision of a "substratum" patterned in very specific ways. *See, e.g.*, Clark, p. 636. Specifically, Clark requires that the substrates were formed with grooves of selected depth and width and "ridges" provided at selected repeat distances. *See, e.g.*, Summary, p. 635, and "Substratum patterning, p. 636. This formed a very regular pattern of grooves, as seen in Figures 2A-2F, 4A-4F, 5A-5D, and 8A-8B. In contrast to the above, the present invention provides substrates with non-uniformly grooved surfaces aligned with an axis of the substrate. *See, e.g.*, Specification, p. 10, lines 17-25. This is further seen in the methods used to produce the textures on metal surfaces which are then transferred to suitable biomaterials for use in creating the devices of the present invention:

> Oriented surface finishes are prepared on appropriate sized electroformed solid nickel, titanium or other suitable machinable metal surface by one of several methods including but not limited to flat lapping, grinding, milling or turning to produce a surface finish with an average surface roughness of at least 4 microinches but not exceeded 64 microinches with a surface texture made in one direction to produce an oriented surface microtextures.

Specification, page 17, line 30 to page 18, line 4. Techniques such as flat lapping, grinding, milling, and turning may provide texture that has a specific directional orientation, as in the present invention, but are generally unsuited for producing structures with regular grooves as taught in Clark. Clark thus teaches production of suitable grooves using photolithographic and dry etching techniques. Clark, p. 636. Clark fails to teach use of a surface topography having non-uniform grooves aligned with an axis of the substrate, and is thus insufficient to support the 35 U.S.C. §102(b) rejection made by the Examiner. Applicants respectfully request withdrawal of this rejection.

Claim Rejections – 35 U.S.C. §103

Under 35 U.S.C. §103(a), a claim is not prima facie obvious unless all of the limitations that are found in the claim are taught or suggested by the cited prior art references. *See* MPEP §2143.03. As amended above, claims 1 and 8 state that surface topographies of the devices of the present invention, when used, include "non-uniform grooves substantially aligned with the axis of the substrate." *See, e.g.,* claims 1 and 8, *supra*. The Clark reference cited by the Examiner fails to teach this feature. Neither Ricci, Curtis, nor Naughton teach this limitation. As a result, the combination fails to establish *prima facie* obviousness of claims 1-19, 21, 26, and 31-37, and the rejection should be withdrawn.

Claim 20 was additionally rejected under 35 U.S.C. §103(a) as being unpatentable over Clark, Ricci, Curtis, and Naughton in further view of Vandenburgh. As with the previous §103 rejection, all of the claim limitations are not taught by the cited art, and thus the rejection is improper.

Applicants respectfully request that a timely Notice of Allowance be issued in this case. If there are any remaining issues preventing allowance of the pending claims that may be clarified by telephone, the Examiner is requested to call the undersigned.

Respectfully submitted,

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metals) in manufacturing and subsequent performance in service. The scope of surface integrity is usually interpreted to include surface texture, as well as the altered layer beneath.

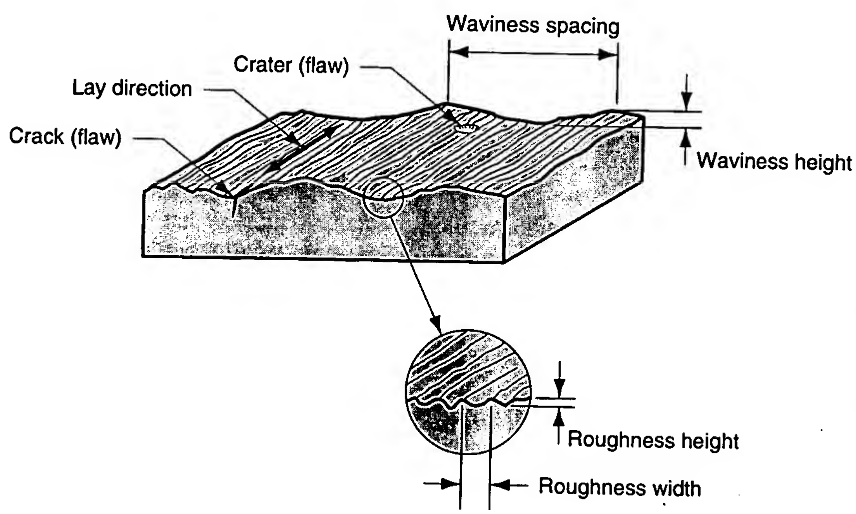
In addition to the surface texture and altered layer beneath, other features may also characterize the surface. Most metal surfaces are coated with an *oxide film*, given sufficient time after processing for the film to form. Aluminum forms a hard, dense, thin film of Al_2O_3 on its surface (which serves to protect the substrate from corrosion), and iron forms oxides of several chemistries on its surface (rust, which provides virtually no protection at all). There is also likely to be moisture, dirt, oil, adsorbed gases, and other contaminants on the part's surface.

5.2.2 Surface Texture

Surface texture consists of the repetitive and/or random deviations from the nominal surface of an object; it is defined by four elements: roughness, waviness, lay, and flaws. These features are illustrated in Figure 5.3. *Roughness* refers to the small, finely spaced deviations from the nominal surface that are determined by the material characteristics and the process that formed the surface. *Waviness* is defined as the deviations of much larger spacing; they occur due to work deflection, vibration, heat treatment, and similar factors. Roughness is superimposed on waviness. *Lay* is the predominant direction or pattern of the surface texture. It is determined by the manufacturing method used to create the surface, usually from the action of a cutting tool. Figure 5.4 presents most of the possible lays a surface can take, together with the symbols used by a designer to specify them. Finally, *flaws* are irregularities that occur occasionally on the surface; these include cracks, scratches, inclusions, and similar defects in the surface. Although some of the flaws relate to surface texture, they also affect surface integrity (Section 5.2.3).

Surface Roughness and Surface Finish These are two terms included within the scope of surface texture. Surface roughness is a measurable characteristic based on the roughness deviations as defined previously. *Surface finish* is a more subjective term denoting smoothness and general quality of a surface. In popular usage, surface finish is often used as a synonym for surface roughness.

FIGURE 5.3 Surface texture features.



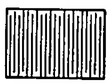
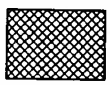
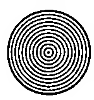
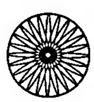
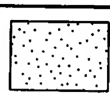
Lay symbol	Surface pattern	Description
=		Lay is parallel to line representing surface to which symbol is applied.
⊥		Lay is perpendicular to line representing surface to which symbol is applied.
X		Lay is angular in both directions to line representing surface to which symbol is applied.
M		Lay is multidirectional.
C		Lay is circular relative to center of surface to which symbol is applied.
R		Lay is approximately radial relative to the center of the surface to which symbol is applied.
P		Lay is particulate, nondirectional, or protuberant.

FIGURE 5.4 Possible lays of a surface. Source: [1].

The most commonly used measure of surface texture is surface roughness. With respect to Figure 5.5, *surface roughness* can be defined as the average of the vertical deviations from the nominal surface over a specified surface length. An arithmetic average (AA) is generally used, based on the absolute values of the deviations, and this roughness value is referred to by the name *average roughness*. In equation form,

$$R_a = \int_0^{L_m} \frac{|y|}{L_m}\, dx \tag{5.1}$$

where R_a = arithmetic mean value of roughness, in. (m); y = the vertical deviation from nominal surface (converted to absolute value), in. (m); and L_m = the specified distance

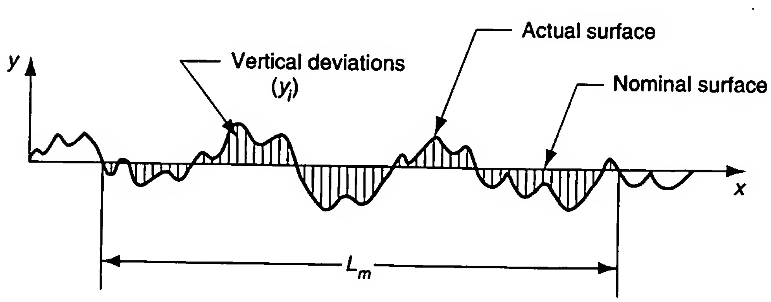


FIGURE 5.5 Deviations from nominal surface used in the two definitions of surface roughness.

over which the surface deviations are measured. An approximation of Eq. (5.1), perhaps easier to comprehend, is given by

$$R_a = \sum_{i=1}^{n} \frac{|y_i|}{n} \tag{5.2}$$

where R_a has the same meaning as before; y_i = vertical deviations (converted to absolute value) identified by the subscript i, in. (m); and n = the number of deviations included in L_m. We have indicated that the units in these equations are inches (m). In fact, the scale of the deviations is very small, so more appropriate units are microinches (inch $\times$ 10^{-6}) and micrometers (m $\times$ 10^{-6} or mm $\times$ 10^{-3}). These are the units commonly used to express surface roughness.

The AA method is the most widely used averaging method for surface roughness today. An alternative, sometimes used in the United States, is the *root-mean-square* (rms) average, which is the square root of the mean of the squared deviations over the measuring length. RMS surface roughness values will almost always be greater than the AA values. This is because the larger deviations will figure more prominently in the calculation of the rms value.

Surface roughness suffers the same kinds of deficiencies as any single measure used to assess a complex physical attribute. For example, it fails to account for the lay of the surface pattern; thus, surface roughness may vary significantly depending on the direction in which it is measured.

Another deficiency is that waviness can be included in the R_a computation. To deal with this problem, a parameter called the *cutoff length* is used as a filter that separates the waviness in a measured surface from the roughness deviations. In effect, the cutoff length is a sampling distance along the surface. A sampling distance shorter than the waviness width will eliminate the vertical deviations associated with waviness and only include those associated with roughness. The most common cutoff length used in practice is 0.030 in. (0.8 mm). The measuring length L_m is normally set at about five times the cutoff length.

Symbols for Surface Texture Designers specify surface texture on an engineering drawing by means of symbols as in Figure 5.6. The symbol designating surface texture parameters is a check mark (looks like a square root sign), with entries as indicated for average roughness, waviness, cutoff, lay, and maximum roughness spacing. The symbols for lay are from Figure 5.4.

FIGURE 5.6 Surface texture symbols in engineering drawings: (a) the symbol and (b) symbol with identification labels. Values of R_a are given in microinches; units for other measures are given in inches. Designers do not always specify all the parameters on engineering drawings.